K951459

510(k) Summary

JUL 14 1997

SUBMITTER: Ortho Diagnostic Systems Inc.
1001 U.S. Highway 202
Raritan, NJ 08869-0606

CONTACT: Gail Kromer
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DEVICE NAME: Ortho-mune™OKT™4A (CD4) Monoclonal Antibody (Murine) FITC Conjugate

PREDICATE: CD4(Leu™-3a) FITC

DATE: July 8, 1997

DEVICE DESCRIPTION

Ortho-mune OKT4A Monoclonal Antibody (Murine) FITC Conjugate contains the purified monoclonal antibody OKT4A conjugated to the fluorochrome fluorescein isothiocyanate.

INTENDED USE:

Ortho-mune OKT4A FITC Conjugate is intended for use in identification and enumeration of CD4+ human T lymphocytes in whole blood by flow cytometry. The intended use is the same as the intended use of the predicate device, CD4 (Leu-3a) FITC commercially distributed by Becton Dickinson Immunocytometry Systems.

TECHNOLOGICAL CHARACTERISTICS

Both Ortho-mune OKT4A Monoclonal Antibody (Murine) FITC Conjugate and CD4 (Leu-3a) FITC utilize monoclonal antibodies specific for human helper/inducer T cells OKT4A/Leu-3a) respectively, conjugated to the same fluorochrome, fluorescein isothiocyanate.

PERFORMANCE CHARACTERISTICS

Performance of Ortho-mune OKT4A Monoclonal Antibody (Murine) FITC Conjugate was compared with that of CD4 (Leu-3a) FITC at three external, geographically distinct sites. Whole blood specimens from 206 normal donors, and 88 AIDS/ARC patients were stained and analyzed using the ORTHO CYTORONABSOLUTE™ flow cytometer, Ortho Diagnostic Systems Inc.

For each specimen, the percentage of gated cells which showed positive by each marker was calculated. The mean and range of the percent CD4+ cells for the normal donor and AIDS/ARC population are shown in Table 1 and Table 2 respectively.

TABLE 1

PERCENT POSITIVE STAINED CELLS IN NORMAL DONORS DETECTED BY OKT4A AND LEU-3A ASSAYED ON THE CYTORONABSOLUTE
N=206

Ortho-mune Reagent	Mean %	Range %	BD Reagent	Mean %	Range %
OKT4A (CD4)+	47.0	12.4 - 68.7	LEU-3a (CD4)+	45.1	14.6 - 64.6

TABLE 2

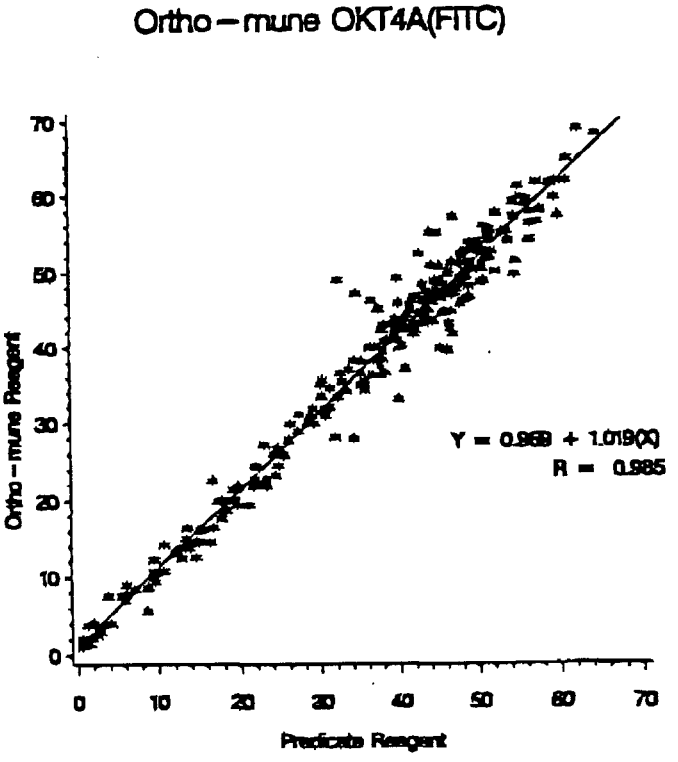
PERCENT POSITIVE STAINED CELLS IN AIDS/ARC PATIENTS DETECTED BY OKT4A AND LEU-3A ASSAYED ON THE CYTORONABSOLUTE
N=88

Ortho-mune Reagent	Mean %	Range %	BD Reagent	Mean %	Range %
OKT4 (CD4)+	18.3	1.0 - 55.1	LEU-3a (CD4)+	17.2	0.6 - 51.6

Linear regression analysis of total percent CD4+ cells from the combined normal and AIDS/ARC populations is found in Chart 1.

CHART 1

Ortho-mune OKT4A (CD4) FITC vs CD4 (Leu-3a) FITC



This study demonstrates that the performance of Ortho-mune OKT4A (CD4) Monoclonal Antibody (Murine) FITC Conjugate is equivalent to CD4 (Leu-3a) FITC reagent in identification and enumeration CD4+ human lymphocytes in whole blood by flow cytometry.

WITHIN-LABORATORY REPRODUCIBILITY

Ten normal donors were used in a within-laboratory reproducibility study at three independent laboratories. The samples were processed using antibody-coated magnetic microbeads to produce low, normal and high percent positive CD4 populations to simulate leukopenia and leukocytosis. The samples were stained with Ortho-mune OKT4A (CD4) FITC Conjugate and run on the ORTHO CYTORONABSOLUTE. All samples were analyzed in replicates of ten. The coefficients of variation, calculated from the standard deviation between replicates, were compared and demonstrated excellent within-laboratory reproducibility at all concentrations tested. The 95% confidence intervals were calculated from the standard error of the site mean which includes variance components from replicate and donor variability minimized by the number of donors (10). The comparison of normal, concentrated (high) and diluted (low) samples is contained in Table 3.

TABLE 3: N = 10
WITHIN-LABORATORY REPRODUCIBILITY
Ortho-mune OKT4A (CD4) FITC CONJUGATE
PERCENT POSITIVE RESULTS

CD4 Level	Low			Normal			High		
Subset: OKT4A (CD4)	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
Mean Percent Positive	9.60	9.36	8.86	47.38	47.19	48.54	56.13	55.83	56.50
CV	7.60	6.12	5.47	2.33	2.00	2.21	1.93	1.79	2.09
+/- 95% Confidence Interval	4.18	3.53	3.45	3.74	3.84	4.22	4.93	4.91	5.15

BETWEEN-LABORATORY REPRODUCIBILITY

Ten normal donor samples were compared between three independent laboratories. The samples were processed using antibody-coated magnetic microbeads to produce low, normal and high percent positive CD4 populations. The samples were stained with Ortho-mune OKT4A (CD4) FITC Conjugate and run on the ORTHO CYTORONABSOLUTE. All samples were analyzed in replicates of ten. The between-laboratory coefficient of variation (CV) and the 95% confidence intervals were calculated from the standard deviation between site means. The data collected from all sites are shown in Table 4. The data show excellent between-laboratory reproducibility.

TABLE 4: N = 10
BETWEEN-LABORATORY REPRODUCIBILITY
Ortho-mune OKT4A (CD4) FITC CONJUGATE
PERCENT POSITIVE RESULTS

CD4 Level	Low	Normal	High
Mean Percent Positive	9.25	47.70	56.15
CV	4.09	1.53	0.60
+/- 95% Confidence Interval	1.63	3.14	1.46

Ortho-mune OKT4A (CD4) Monoclonal Antibody (Murine) FITC Conjugate immunophenotyping reagent shows acceptable within and between laboratory reproducibilty for determination of CD4+ lymphocyte percentages.

A linearity study was performed using an automated hematology analyzer to determine total lymphocyte count, and the CYTORONABSOLUTE flow cytometer to determine the percent positive CDx cells.

Specimens from four normal donors (whole blood, EDTA) were processed to produce samples with low, normal and high numbers of lymphocyte subsets. Each whole blood specimen was concentrated by harvesting the buffy coat to obtain a white blood cell count between 20,000 and 40,000 cells/ul and then diluting to produce samples of high, normal and low numbers of lymphocyte subsets. A portion of each sample was stained in triplicate using Ortho-mune OKT4A (CD4) FITC Conjugate immunophenotyping reagent and analyzed using the CYTORONABSOLUTE flow cytometer. The total lymphocyte count of the concentrated sample for each donor was obtained using an automated hematology analyzer.

Linear regression analyses were performed as follows. The expected (X axis) values were calculated by multiplying the corresponding serial dilutions by the hematology analyzer derived buffy coat lymphocyte count and by the CYTORONABSOLUTE derived lymphocyte subset percent positive. The observed (Y axis) values were determined as the total lymphocyte count calculated from the hematology derived value of the concentrated sample times the CYTORONABSOLUTE derived lymphocyte subset percent positive at each dilution.

The Ortho-mune OKT4A (CD4) FITC Conjugate reagent demonstrated linear performance for total CD4+ lymphocyte subsets across a lymphocyte count range of 20 cells/uL to 9000 cells/uL as demonstrated with slopes indistinguishable from 1 and R values of 1.000.

Linear regression analyses of observed versus expected values for total percent CD4+ cells for each donor specimen are shown in. Regression analysis statistics are provided in Table 5.

CHART 2

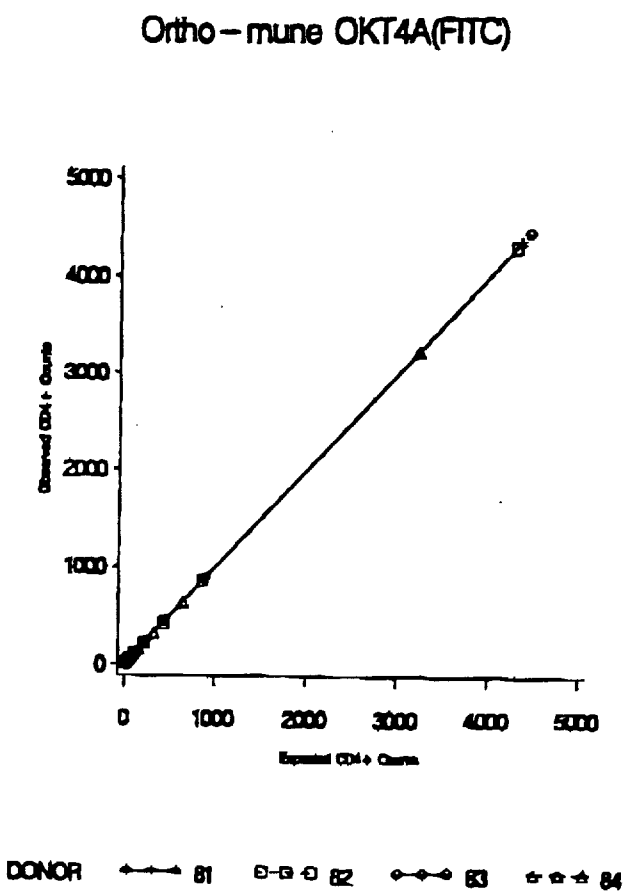

Ortho – mune OKT4A(FITC)
5000
4000
3000
2000
1000
0
0
1000
2000
3000
4000
5000
DONOR
81
82
83
84

TABLE 5

LINEARITY (Ortho-mune OKT4A FITC) N = 4						
Ortho-mune	Donor	SLOPE	CI	INTERCEPT	CI	R
TOTAL $CD4^+$	1	0.999	0.003	6.099	5.242	1.000
TOTAL $CD4^+$	2	1.000	0.001	0.395	2.226	1.000
TOTAL $CD4^+$	3	0.999	0.003	4.449	4.176	1.000
TOTAL $CD4^+$	4	1.000	0.001	0.285	1.316	1.000
TOTAL $CD4^+$	All	0.999	0.001	2.777	1.655	1.000

CONCLUSION

Performance of Ortho-mune OKT4A (CD4) Monoclonal Antibody (Murine) FITC Conjugate is substantially equivalent to CD4 (Leu-3a) FITC reagent in the identification and enumeration of CD4+ human T lymphocytes in whole blood by flow cytometry.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Ms. Gail Kromer
Manager, Regulatory Affairs
Ortho Diagnostic Systems, Inc.
1001 U.S. Highway 202
Raritan, New Jersey 09969-0606

JUL 14 1997

Re: K951459/S3
Trade Name: Ortho-mune™ OKT™4A (CD4) Monoclonal Antibody (Murine) FITC Conjugate
Regulatory Class: II
Product Code: GKZ
Dated: April 21, 1997
Received: April 23, 1997

Dear Ms. Kromer:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the current Good Manufacturing Practice requirement, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic (QS) inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html"

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Indications for Use Statement

510(k) Number (if known) K951459

Device Name: Ortho-mune™OKT™4A (CD4)
Monoclonal Antibody (Murine) FITC Conjugate

Indications for Use: Ortho-mune OKT4A (CD4) Monoclonal Antibody (Murine) FITC Conjugate is used to identify and enumerate the percentage of CD4+ human T lymphocytes in whole blood by flow cytometry.

Identification and enumeration of abnormal levels of CD4lymphocytes may be clinically significant in the prognosis of secondary immunodeficiency diseases (acquired immunodeficiency syndrome [AIDS]).

AIDS is characterized by a severe reduction in T helper CD3+CD4+) lymphocytes and a decrease in the CD4:CD8 ratio. The CD4:CD8 ratio has been used as a predictor of time to the development of AIDS. CD4 counts should also be determined using a CD3/CD4 combination reagent to eliminate monocyte contamination (CD3-CD4+dim). CD4+lymphocytes (expressed as an absolute number, a percentage of lymphocytes or as a ratio of CD4+ to CD8+ T lymphocytes) represents the best single predictor of the progression of AIDS. CD4+ lymphocyte numbers usually start to decline relatively soon after human immunodeficiency virus (HIV) infection.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)
Division Sign-Off
Division of Clinical Laboratory Devices
510(k) Number

Prescription Use ✓ **OR** **Over-The-Counter-Use** ____

(Per 21 CFR 801.109) (Optional Format 1-2-96)